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09/762,243	02/05/2001	Yoram Kapulnik	01/21632	2822

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EXAMINER

KUBELIK, ANNE R

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 03/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

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## Office Action Summary

### Application No.

09/762,243

### Applicant(s)

KAPULNIK ET AL.

### Examiner

Anne R. Kubelik

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 06 January 2004 and 10 February 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 54-60 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 54-60 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 06 January 2004 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- 1) ☐ Certified copies of the priority documents have been received.
  - 2) ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - 3) ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date. _____  | 6) <input type="checkbox"/> Other: _____                                    |

### DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10 February 2004 has been entered.
2. Claims 54-60 are pending.
3. The amendment to the claims filed 6 January do not follow the Revised Amendment Practice of 37 CFR 1.121. Specifically, the remarks should start on a separate page from the amendments.
4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
5. Color photographs and color drawings, as filed 6 January 2004, are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) is granted permitting their use as acceptable drawings. In the event that applicant wishes to use the drawings currently on file as acceptable drawings, a petition must be filed for acceptance of the color photographs or color drawings as acceptable drawings. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and an amendment to the first paragraph of the brief description of the drawings section of the specification which states:

The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the U.S. Patent and Trademark Office upon request and payment of the necessary fee.

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Color photographs will be accepted if the conditions for accepting color drawings have been satisfied.

6. The rejection of claims 1-2, 4, 6-7, 9-14, 18-22, 24-29, 31-33, 35-38 and 50-51 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention does not apply to the instant claims as they are limited to expressing streptavidin in plants.

7. The rejection of claims 2, 7, 19, 22, 31 and 33 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention does not apply to the instant claims.

8. The rejection of claims 1-2, 4, 6-7, 9, 13-14, 18-22, 24, 28-29, 31-33, 38 and 50 under 35 U.S.C. 102(b) as being anticipated by Howard et al (WO 96/40949) does not apply to the instant claims as they are limited to expressing streptavidin in plants.

9. The rejection of claims 1-2, 4, 6-7, 9, 12-14, 18-22, 24, 27-29, 31-33, 37-38 and 50 under 35 U.S.C. 102(b) as being anticipated by Baszczynski et al (1998, US Patent 5,767,379) does not apply to the instant claims as they are limited to expressing streptavidin in plants.

10. The rejection of claims 1-2, 4, 6-7, 9-14, 18-22, 24-29, 31-33, 36-38 and 50-51 under 35 U.S.C. 103(a) as being unpatentable over Baszczynski et al (1998, US Patent 5,767,379 in view of Mariani et al (1997, US Patent 5,689,041) does not apply to the instant claims as they are limited to expressing streptavidin in plants.

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11. The rejection of claims 1-2, 4, 6-7, 9-10, 12-14, 18-22, 24-25, 27-29, 31-33, 35, 37-38 and 50 under 35 U.S.C. 103(a) as being unpatentable over Baszczynski et al (1998, US Patent 5,767,379 in view of Maliga et al (1996, US Patent 5,530,191) does not apply to the instant claims as they are limited to expressing streptavidin in plants.

***Claim Rejections - 35 USC § 112***

12. Claim 56 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Neither the instant specification nor the originally filed claims appear to provide support for the phrase "wherein said viable plants are male fertile" in claim 56. Thus, such a phrase constitutes NEW MATTER. In response to this rejection, Applicant is required to point to support for the phrase or to cancel the new matter.

13. Claim 55 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 11 August 2003, as applied to claims 1-2, 4, 5-7, 9-14, 18-22, 24-29, 31-33, 35-38 and 50-51. Applicant's arguments filed 6 January 2004 have been fully considered but they are not persuasive.

Neither the instant specification nor the originally filed claims appear to provide support for the phrase "vegetative plant tissue". The specification states that the invention is drawn to a method of effecting degeneration of somatic plant tissue (pg 2, lines 12-13), and "somatic" is defined as referring to both vegetative and reproductive plant tissues, not either vegetative or reproductive plant tissues (pg 25, lines 10-13). Thus, such a phrase constitutes NEW MATTER. In response to this rejection, Applicant is required to point to support for the phrase or to cancel the new matter.

Applicant urges that pg 25, lines 10-14 of the published PCT defines somatic and vegetative tissue and the Examples illustrate selective degeneration of vegetative tissue, for example degeneration of young leaves in Figure 5 and 7. Thus, applicant urges that the specification clearly defines to the ordinary skilled artisan what such tissue constitutes and how to generate and select such plants (response pg 3).

This is not found persuasive. The specification states that the invention is drawn to a method of effecting degeneration of somatic plant tissue (pg 2, lines 12-13), and "somatic" is defined as referring to both vegetative and reproductive plant tissues, not either vegetative or reproductive plant tissues (pg 25, lines 10-13). Thus, the invention as originally filed is not drawn to use only in vegetative tissue.

14. Claims 54-60 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of using streptavidin-encoding constructs with the  $\alpha\beta$  gliadin storage protein signal sequence for secretion and the streptavidin processing sequences, and with and without the bacterial streptavidin signal peptide, expressed from a constitutive promoter, to transform plants, and plants so obtained, does not reasonably provide enablement for constructs

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methods of using streptavidin-encoding constructs without a secretion signal sequence or streptavidin with the processing sequences to transform plants, plants so obtained, or methods of mitochondria transformation with a construct encoding streptavidin. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is modified from the rejection set forth in the Office action mailed 11 August 2003, as applied to claims 1-2, 4, 6-7, 9-14, 18-22, 24-29, 31-33, 35-38 and 50-51. Applicant's arguments filed 6 January 2004 have been fully considered but they are not persuasive.

The claims are broadly drawn to methods of using streptavidin-encoding constructs without a secretion signal sequence or streptavidin with the processing sequences to transform plants, plants so obtained, or methods of mitochondria transformation with a construct encoding streptavidin.

The instant specification, however, only provides guidance for construction of streptavidin-encoding constructs with and without a plant signal sequence for secretion (the (xp gliadin storage protein signal sequence), the bacterial streptavidin signal peptide, and the streptavidin processing sequences, expressed from the CaMV 35S promoter (Figure 2, pg 43-44), their transformation into tomato (pg 44) and testing for the presence of the streptavidin gene in transformants by PCR, and Southern and Northern blotting (pg 44-46). Only the constructs that comprised a plant signal sequence for secretion and the streptavidin processing sequences did not cause severe necrosis (pg 46-47), and plants transformed with a construct comprising a plant signal sequence for secretion, the bacterial streptavidin signal peptide, and the streptavidin processing sequences were analyzed further - most died before maturity and/or displayed

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abnormal morphology, but spraying biotin on the plants stopped degeneration (pg 47-48 and 50). Seeds from the plants had reduced germination that could be restored by application of biotin (pg 49). Plants transformed with a construct encoding streptavidin expressed from the root specific Tob promoter were female sterile and had fruit tissue degeneration (pg 48).

The instant specification fails to provide guidance for methods of using streptavidin-encoding constructs without a secretion signal sequence or streptavidin with the processing sequences to transform plants, plants so obtained, or methods of mitochondria transformation with a construct encoding streptavidin.

The specification, on pg 24, lines 10-11, states "As used herein and in the claims section which follows, the phrase 'DNA containing organelle' refers to mitochondria and chloroplasts." Thus, claim 59 is drawn to a method of transforming plant mitochondria. However, transformation of mitochondria is not known in the art and is not taught in the specification. Thus, undue experimentation would be required to transform the constructs into plant mitochondria to produce plants with degenerated somatic tissue, if such plants could even be generated.

The examples in the specification teach that a plant signal sequence for secretion is an essential feature of the constructs, as all seedlings transformed with a construct without this sequence died (see, e.g., pg 46, lines 19-29, and table 3). This essential feature is missing from the constructs of the claims. It is also not clear that constructs wherein the streptavidin is linked to a chloroplast or mitochondria targeting sequence will produce live plants, as chloroplasts and mitochondria have numerous biotin-requiring biochemical pathways that when interrupted may also result in dead plants.



Generation of plants that had fruit tissue degeneration required expressing streptavidin from the root specific Tob promoter (pg 48). It is not clear that such plant could be generated without use of a root-specific promoter.

Given the claim breath, undue experimentation, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

Applicant urges that the claims are now limited to use of streptavidin (response pg 4).

This is not found persuasive because the specification does not teach transformation of mitochondria. The specification also teaches that a plant signal sequence for secretion is an essential feature of the constructs.

#### ***Claim Rejections - 35 USC § 102***

15. Claims 54-56 are rejected under 35 U.S.C. 102(e) as being anticipated by Albertson et al (US Patent 5,962,769, filed July 1997). The rejection is repeated for the reasons of record as set forth in the Office action mailed 11 August 2003, as applied to claims 1-2, 4, 6-7, 9, 12-14, 18-22, 24, 27-29, 31-33, 37-38 and 50. Applicant's arguments filed 6 January 2004 have been fully considered but they are not persuasive.

Albertson et al teach transformation of plants with a nucleic acid comprising a sequence encoding a signal sequence for secretion (the barley alpha amylase signal sequence) and a sequence encoding a biotin-binding protein (avidin or streptavidin), expressed from an anther-specific promoter or the constitutive ubiquitin promoter (claims 1-42, column 7, lines 49-56, column 18, line 49, to column 20, line 11). Such expression leads to male sterility because of degeneration of tissue and would result in control morphology and development of the plant.

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Anther tissue is somatic because it is not germ-line tissue. Plant viability is maintained (see, e.g., column 20, lines 1-11). Anther-specific promoters like the maize 5126 promoter, the maize SGB6 promoter, and the maize G9 promoter, are plant derived (column 12, line 14, to column 13, line 48). Plants that are further sprayed with biotin are male fertile (column 15, lines 51-63).

Applicant urges that the instant invention is drawn to method for controlling plant morphology via selective somatic plant tissue degeneration. Applicant urges that the prior art methods do not employ or suggest a step of identifying and selecting plants that exhibit altered morphology as a result of somatic degeneration and that the claims have been amended to recite that the selected plants exhibit degeneration of the selected tissue. Applicant urges that the selection step is pivotal as expression of streptavidin does not produce progeny with uniform morphology and may lead to plant death (response pg 4-5).

This is not found persuasive. Male sterility is a morphological characteristic that can be observed (see Albertson et al, column 19, lines 63-67) and plants were selected (ibid). Albertson et al teaches expression of a sequence encoding a biotin-binding protein from the constitutive ubiquitin promoter. The constitutive ubiquitin promoter causes expression in all, or almost all plant tissues, and would thus cause expression of the protein in vegetative tissue.

### ***Claim Rejections - 35 USC § 103***

16. Claims 54-56 and 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Albertson et al (US Patent 5,962,769, filed July 1997) in view of Mariani et al (1997, US Patent 5,689,041).

The claims are drawn to a method of generating a plant having degenerated somatic tissue by expressing streptavidin in cells of the plant and selecting viable plants that have degeneration of the tissue, wherein the streptavidin is targeted to a DNA-containing organelle.

The teachings of Albertson et al are discussed above. Albertson et al does not disclose targeting the streptavidin to a DNA-containing organelle.

Mariani et al teach a method of effecting degeneration of somatic plant tissue by transformation with a nucleic acid comprising construct encoding a toxic protein (barstar) operably linked to a plastid or mitochondrial targeting sequence, such that the toxic protein is expressed in plastids or mitochondria (claims 3 and 30).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of effecting degeneration of somatic plant tissue taught by Albertson et al, to target the protein to the plastid as described in Mariani et al. One of ordinary skill in the art would have been motivated to do so because substitution of one toxic protein for another toxic protein is an obvious design choice.

17. Claims 54-56 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Albertson et al (US Patent 5,962,769, filed July 1997) in view of Maliga et al (1996, US Patent 5,530,191).

The claims are drawn to a method of generating a plant having degenerated somatic tissue by expressing streptavidin in cells of the plant and selecting viable plants that have degeneration of the tissue, wherein the streptavidin is expressed in a DNA-containing organelle.

The teachings of Albertson et al are discussed above. Albertson et al does not disclose expressing streptavidin in a DNA-containing organelle.

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Maliga teaches a method of effecting degeneration of somatic plant tissue by plastid transformation with a nucleic acid comprising a sequence a toxic protein, including an RNase, a protease, and a DNase, such that the toxic protein is expressed in plastids (claims 1-18).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of effecting degeneration of somatic plant tissue taught by Albertson et al, to express the protein in the plastid as described in Maliga. One of ordinary skill in the art would have been motivated to do so because substitution of one toxic protein for another toxic protein is an obvious design choice.

18. Claims 57-58 are free of the prior art, given the failure of the prior art to teach or suggest a method of generating a plant having degenerated somatic tissue by expressing streptavidin in cells of the plant and selecting viable plants that have degeneration of the tissue, wherein the plants are selected for degeneration of embryo tissue, or young leaf tissue and/or shoots.

### *Conclusion*

19. No claim is allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (571) 272-0547.

Anne R. Kubelik, Ph.D.  
March 24, 2004



ANNE KUBELIK  
PATENT EXAMINER